Comparison of Two Linear Models of Dynamic Cerebral Autoregulation

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Abstract- **The assessment of dynamic cerebral autoregulation response using changes in arterial blood pressure (ABP) as a stimulus is increasingly used. Transcranial Doppler ultrasonography measurements of middle cerebral artery velocity (MCAv) are often used in conjunction with ABP measurements using photoplethysmography (e.g. Finapres) to assess the response of the autoregulation mechanism. Two linear models of dynamic cerebral autoregulation have been developed independently. The first is an ARX model using the least-squares algorithm to fit the ABP and MCAv signals. The second is a flow dependent feedback mechanism controlling the pressure gradient across the MCA. Both models have been found to reproduce qualitatively similar results to those recorded in both thigh cuff and lower body negative pressure experiments, whereas the first model has also been used to analyse MCAv simulated using Ursino's physiological model. This paper assesses the ability of the two models to reproduce MCAv measurements from recordings of ABP from the same experiments.**

Keywords- **Cerebral autoregulation, System identification, Physiological simulation, Modeling**

I. INTRODUCTION

Cerebral autoregulation, the active changes in arterial and arteriolar diameters, allows cerebral blood flow (CBF) to be maintained despite changes in cerebral perfusion pressure. Both arterial blood pressure (ABP) and middle cerebral arterial flow velocity (MCAv) can be measured noninvasively using photoplethysmography (e.g. Finapres) and transcranial Doppler ultrasonography (TCD) respectively. Recent studies show that the mean MCAv variability is largely due to the spontaneous changes in ABP, providing the other physiological conditions are in a steady state, e.g. arterial pCO_2 is constant [1], [2].

Many types of experiment have been developed to manipulate the ABP in order to assess dynamic autoregulation, such as the thigh cuff technique and carotid artery compression to create step changes in ABP together with controlled breathing, squat-standing and lower body negative pressure (LBNP) experiments that induce slow oscillatory variations in ABP [3]. Data from both the thigh cuff and LBNP techniques are used in this paper to investigate the variability in ABP and MCAv.

Many different approaches have been adopted to establish a quantitative relationship between ABP and MCAv [4], [5]. In this paper, two different linear mathematical models of dynamic autoregulation are presented.

The first approach is ARX modeling. The ARX model is constructed using the least-squares algorithm to fit MCAv data by the simultaneous ABP data. Besides collecting MCAv from TCD, MCAv is also simulated by a physiological model. The multi-compartmental physiological model developed by Ursino and his colleagues [6] is used to simulate a controllable cerebral circulation system, i.e. we can change the cerebral autoregulation by adjusting some parameters of the physiological model. This physiological model simulation showed a good correspondency with real MCAv [7]. The step response of ARX models constructed using different ABP data are analyzed.

The second modelling approach represents the autoregulation as a flow dependent feedback mechanism that is assumed to alter the pressure gradient along the MCA, modelled as a long rigid pipe. This pressure gradient, in turn, drives the flow through the MCA from which MCAv can be calculated.

Both studies assume that MCAv is reasonably consistent with cerebral blood flow (CBF), despite the fact that there may be a slight change in diameter of the middle cerebral arteries (MCA) caused by a change of intracranial pressure (ICP).

II. METHODOLOGY

A. *Experimental measurements*

Two experimental procedures were carried out to assess dynamic autoregulation in the present study. ABP was monitored using a Finapres and MCAv was simultaneously recorded using TCD in both procedures. The sampling rate was 20Hz. Data was collected from three healthy volunteers having no history of vascular disease. Each experiment was repeated six times in each volunteer.

The first procedure is the thigh cuff technique, which has been widely used and described in many studies. The mean±SD duration of the 6×3 records analyzed was 85±14 sec.

The second set of experiments used the LBNP box currently being developed at Southampton General Hospital. A lower body negative pressure is varied sinusoidally to produce oscillatory variations in ABP with amplitude of 5-

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Abstract

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10% of the mean and a period of 12 sec. The mean±SD duration of the LBNP box experiments was 300±25 sec.

B. MCAv simulation

The physiological model of cerebral hydrodynamics was proposed in a series of papers by Ursino and his colleagues [6], [7], [8]. We have implemented the model on a PC using the Matlab-Simulink software package. The ABP is the input to the model and the relative changes in simulated cerebral dynamics, e.g. ICP and MCAv can be observed in real-time. Four ABP data sets recorded in each of above experiments were randomly selected to be the input of the physiological model.

Some parameters significantly influencing cerebral autoregulation were set to simulate different regulatory grades, i.e. strong, average, slow and completed impaired autoregulation. Four MCAv responses were recorded for every ABP input.

C. Signal processing

The ABP and MCAv signals were sampled at 20Hz and the beat-to-beat pulsatilities were removed using a seventh-order elliptic low-pass filter. The pass band frequency is 0.5Hz and the stop band frequency is 0.6Hz with –40db attenuation. The ripple amplitude of the pass band is <0.01db. The zero-phase forward and reverse digital filtering technique is applied [9] in order to compensate for the phase shift introduced by the IIR filtering. The data were down-sampled at 1 Hz and 20Hz to be applied to the ARX modeling and flow dependent feedback model respectively.

The ABP and MCAv in each data set were divided by their mean levels in order to compare the relative changes.

D. Parameter estimation of the ARX model

An ARX model, which is also called the Equation Error model, is given by

$$y(t) = \varphi^T(t)\theta + e(t) \qquad (1)$$

where

$$\varphi^T = (-y(t-1)\ldots -y(t-n_a)\ \ u(t-1)\ldots u(t-n_b)) \qquad (1a)$$

and

$$\theta = (a_1 \ldots a_{n_a}\ \ b_1 \ldots b_{n_n})^T \qquad (1b)$$

Here y and u are MCAv and input ABP of the system, respectively whereas *e(t)* is a white-noise term.

The parameter vector, which minimizes the sum of squared equation errors,

$$V_N(\theta) = \frac{1}{N}\sum_{t=1}^{N} e^2(t)$$

is given by

$$\hat{\theta} = \left[\frac{1}{N}\sum_{t=1}^{N}\varphi(t)\varphi^T(t)\right]^{-1}\left[\frac{1}{N}\sum_{t=1}^{N}\varphi(t)y(t)\right] \qquad (1c)$$

E. Flow dependent feedback model

This approach assumes that the MCA is a long straight rigid tube and the flow is fully developed. Therefore the nondimesional linearised Navier-Stokes equations [10] reduces to

$$\frac{\partial^2 v}{\partial r^2} + \frac{1}{r}\frac{\partial v}{\partial r} - \gamma\frac{\partial v}{\partial t} = -4\Delta P \qquad (2a)$$

where $v(r,t)$ is the axial velocity in the MCA, r is the radial position and t is time. The nondimensional parameter $\gamma = a^2/t_0\nu$ where a is the MCA radius, υ is the kinetic viscosity and $t_0 = 1$ is a time constant. The pressure gradient is the sum of three components: $\Delta P_0 = 1$ representing the baseline pressure gradient, ΔP_i the component imposed by the experimental procedure and ΔP_a the component produced by the autoregulation mechanism that is given by

$$\frac{d\Delta P_a}{dt} = \begin{cases} 0, & t < \tau \\ -\lambda(Q^\tau - Q_0), & t \geq \tau \end{cases} \qquad (2b)$$

with $Q^\tau = Q(t-\tau)$ represents the nondimensional volume flow rate at time $t-\tau$ and Q_0 is its baseline value. The two constants λ and τ describe the rate of regulation and time delay of the autoregulation mechanism respectively. Note the nondimesional form has been chosen so that $\mathrm{MCAv} = v(0,t)$ has a baseline value of 1 to allow easy comparison with experimental data.

For each experiment 1024 data points were used, corresponding to 51.15s to allow fast Fourier transforms to be used efficiently. For the thigh cuff experiment the data was selected so that the cuff release occurred at t=10s. For the LBNP experiments the data set was taken from t=120s. The optimal values of model parameters that produced the least mean squared error for 5<t<30s in the thigh cuff experiments and 120<*t*<170.15 for LBNP, were then found for each experiment. Using these parameters the correlation coefficients over 5<t<30 (model 3A) and over all 1024 data points (model 3B) were calculated for the thigh cuff experiments. Only model 3B was used to analyse the LBNP experiments.

III. RESULTS

Table IA and IB presents correlation coefficients between model predicted MCAv from (1) and (2) and the original data. Parameters of models were estimated using the thigh cuff data. The ARX model with n_a=0 and n_b=6 (hereinafter, "Model 1"), i.e. an FIR filter increases the correlation by about 30-80% depending on the level of the correlation of the original data. Model 1 is less data-dependent than the ARX model with n_a=2 and n_b=4 (hereinafter, "Model 2"). Model 2 fits the original data better if the original data is poorly correlated, however, model 2 fails to fit the system when the correlation of the original data is high (Subject 1). The LBNP experiments recorded the data with longer duration and slower variation in both ABP and MCAv. The performance of Model 1is

closely related to the original data in these experiments (Table IB), whereas the performance of Model 2 here is similar to the thigh cuff experiments data set.

The flow dependent feedback model correlates very well with all three subjects over the range $5<t<30$ in the thigh cuff experiments with the release at t=10s (Table IA). However the correlation coefficient is reduced if the larger range $0<t<51.15$ is used. In the analysis of the LBNP box experiments the interval $120<t<171.15$ was analysed as this lay in the middle of each recording. The correlation coefficients (Table IB) were lower than those obtained for the thigh cuff experiment.

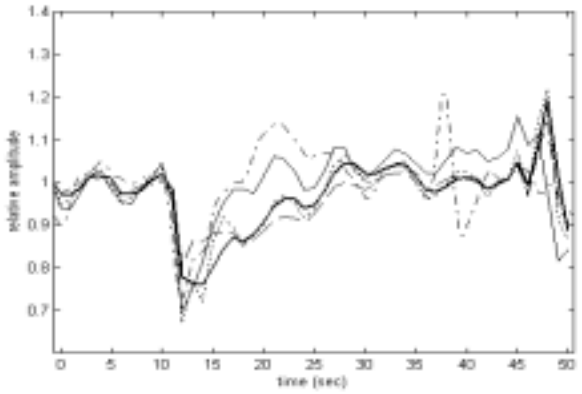

Fig 1. Representative time series of changes in mean ABP (double solid line), MCAv (solid line) and simulated MCAvs using Model 1 (dotted line), Model 2 (dashed line) and Model 3 (dotted-dashed line).

The physiological model simulates a noise-free and steady state cerebral circulation system, i.e. variations in MCAv is merely caused by changes in ABP. Therefore, the model input (ABP) is more strongly correlated with the simulated MCAv. The linear correlation increases as the autoregulation decreases due to the fact that the arteriolar diameter is more passive to the changes in ABP when autoregulation is low (Table II). Model 1 and 2 have similar performances in fitting MCAv, however, Model 2 goes unstable if the system input and output are highly correlated (Subject 4) which causes the singularity of the input auto-correlation matrix (the first part of (1c)).

Fig 1 shows a typical result of three models in the thigh cuff fitting. The ARX model fits the MCAv using a 95-second ABP data set and the performance in modelling the drop in flow velocity is poorer than Model 3A, which models a 25-second ABP data set. Step responses in Fig 2 give a more manifest demonstration that Model 1 (FIR filter) is more sensitive to the abrupt changes in cerebral hydro-dynamics than Model 2 (IIR filter). Additionally, the peak of the Model 1 step responses using the thigh cuff data is 1.98±0.22, whereas the peak using the LBNP data is only 1.60±0.18. The step responses of other subjects are very similar to Fig 2.

Fig 3 presents step responses using the MCAv simulation.

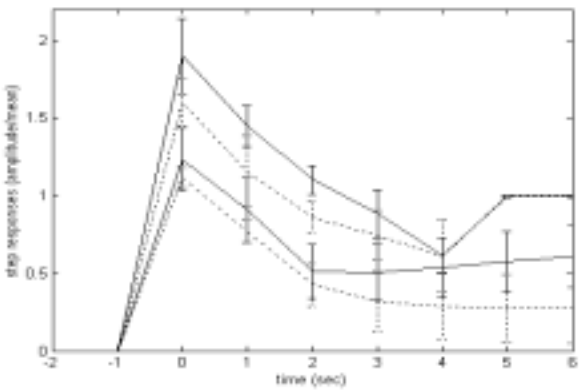

Fig 2. Step responses of the ARX models with SD bars using the thigh cuff (solid lines) and LBNP (dotted lines) data sets. The upper response curve is Model 1 and the lower curve is Model 2 in each set. Data sets used are recorded from the same volunteer (Subject 3).

TABLE IA
MEAN±SD OF CORRELATION COEFFICIENT FOR ALL THIGH CUFF DATA

Subjects	Correlation Coefficient		
	ABP-MCAv	MCAv-MCAv from Model 1*	MCAv-MCAv from Model 2**
1	0.64±0.10	0.77±0.09	0.58±0.21
2	0.38±0.22	0.65±0.15	0.72±0.36
3	0.40±0.35	0.66±0.22	0.75±0.33

TABLE IA CONTINUED

Subject	Correlation Coefficient	
	MCAv-MCAv from Model 3A↑	MCAv-MCAv from Model 3B↑↑
1	0.89±0.12	0.74±0.05
2	0.91±0.07	0.77±0.17
3	0.93±0.07	0.78±0.12

* the ARX model with $n_a=0$ and $n_b=6$ defined in (2)
** the ARX model with $n_a=2$ and $n_b=4$
↑ flow dependent feedback model for $5<t<30$
↑↑ flow dependent feedback model for 1024 data points

TABLE IB
MEAN±SD OF CORRELATION COEFFICIENT FOR ALL LBNP DATA

Subjects	Correlation Coefficient		
	ABP-MCAv	MCAv-MCAv from Model 1*	MCAv-MCAv from Model 2**
1	0.54±0.14	0.61±0.10	0.55±0.15
2	0.20±0.21	0.45±0.24	0.49±0.24
3	0.54±0.13	0.76±0.11	0.73±0.16

TABLE IB CONTINUED

Subject	Correlation Coefficient	
	MCAv-MCAv from Model 3A↑	MCAv-MCAv from Model 3B↑↑
1	N/A	0.62±0.16
2	N/A	0.56±0.17
3	N/A	0.66±0.10

*, **, ↑, ↑↑ the same as TABLE IA

IV. DISCUSSION

The ARX modelling results (Table I and Fig 1) of thigh cuff and LBNP data are consistent with earlier studies [9]. The step responses of ARX model differentiate between

cerebral hydrodynamic systems under different conditions of autoregulation (Fig 3).

In addition, the ARX models obtained from different experiments contain similar information (Fig 1A and 1B), however, the former reflects the stronger responses. The similarity of Fig 3A and Fig 3B suggests that the differences are not due to the differences of the frequency component between two kinds of data, i.e. both thigh cuff and LBNP data have included sufficient information about cerebral autoregulation and therefore both techniques can be used to assess autoregulatory capacity.

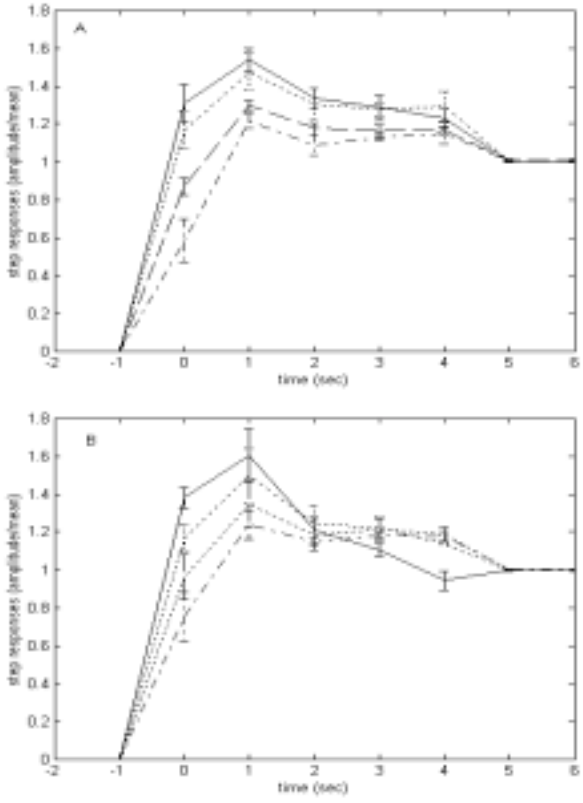

Fig 3. Step responses of the ARX models with SD bars using the physiological simulated MCAv with the thigh cuff (A) and LBNP (B) ABP data inputs. In each plot, the curves from the top to the bottom represent system responses with the strongest to the weakest autoregulation.

In the longer LBNP experiments, changes in MCAv could be subjected to more changes in physiological conditions other than ABP, such as CO2 concentration or metabolic requirement, whereas the physiological simulation assumes those conditions are constant.

The flow dependent feedback model reproduces the thigh cuff experiments very well for $5<t<30$, namely the duration of the response to the thigh cuff release. The ability of the model to reproduce data over a longer time interval is reduced by changes in other physiological parameters that remain relatively constant over the duration of the thigh cuff experiments. This also explains why the correlation for the LBNP box experiments is not as high as in the thigh cuff experiments. In previous work [3] the LBNP box experimental results have been analysed differently. The frequency associated with the ABP oscillations due to the LBNP box were isolated in an attempt to remove the influence of the heart and breathing cycles. This approach may also reduce the influence of variations in other physiological conditions and facilitate easier modelling.

The two models presented here have been developed independently and the intrinsic relationship between the two models has yet to be fully investigated. This will be part of our future study.

TABLE II

MEAN±SD OF CORRELATION COEFFICIENT FOR PHYSIOLGICAL SIMULATION DATA

Subject	Correlation Coefficient using Cuff Thigh Data		
	ABP-MCAv	MCAv-MCAv from Model 1*	MCAv-MCAv from Model 2**
1	0.72±0.12	0.89±0.09	0.90±0.01
2	0.82±0.06	0.93±0.06	0.86±0.09
3	0.92±0.03	0.99±.0.00	0.98±0.01
4	0.98±0.00	0.99±0.00	System unstable

TABLE II CONTINUED

Subject	Correlation Coefficient using LBNP Data		
	ABP-MCAv	MCAv-MCAv from Model 1*	MCAv-MCAv from Model 2**
1	0.78±0.07	0.94±0.05	0.93±0.05
2	0.85±0.08	0.95±0.04	0.94±0.05
3	0.91±0.12	0.97±0.04	0.98±0.02
4	0.97±0.01	0.99±0.01	System unstable

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